

Connecting via Winsock to STN

*STN Process Search
(Casreact)*

Uaim!

Welcome to STN International! Enter x:x

LOGINID:SSPTAJMN1626

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

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* * * * * Welcome to STN International * * * * *

NEWS 1      Web Page for STN Seminar Schedule - N. America
NEWS 2  AUG 06 CAS REGISTRY enhanced with new experimental property tags
NEWS 3  AUG 06 FSTA enhanced with new thesaurus edition
NEWS 4  AUG 13 CA/CAPplus enhanced with additional kind codes for granted
           patents
NEWS 5  AUG 20 CA/CAPplus enhanced with CAS indexing in pre-1907 records
NEWS 6  AUG 27 Full-text patent databases enhanced with predefined
           patent family display formats from INPADOCDB
NEWS 7  AUG 27 USPATOLD now available on STN
NEWS 8  AUG 28 CAS REGISTRY enhanced with additional experimental
           spectral property data
NEWS 9  SEP 07 STN AnaVist, Version 2.0, now available with Derwent
           World Patents Index
NEWS 10 SEP 13 FORIS renamed to SOFIS
NEWS 11 SEP 13 INPADOCDB enhanced with monthly SDI frequency
NEWS 12 SEP 17 CA/CAPplus enhanced with printed CA page images from
           1967-1998
NEWS 13 SEP 17 CAPplus coverage extended to include traditional medicine
           patents
NEWS 14 SEP 24 EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS 15 OCT 02 CA/CAPplus enhanced with pre-1907 records from Chemisches
           Zentralblatt
NEWS 16 OCT 19 BEILSTEIN updated with new compounds
NEWS 17 NOV 15 Derwent Indian patent publication number format enhanced
NEWS 18 NOV 19 WPIX enhanced with XML display format
NEWS 19 NOV 30 ICSD reloaded with enhancements
NEWS 20 DEC 04 LINPADOCDB now available on STN
NEWS 21 DEC 14 BEILSTEIN pricing structure to change
NEWS 22 DEC 17 USPATOLD added to additional database clusters
NEWS 23 DEC 17 IMSDRUGCONF removed from database clusters and STN
NEWS 24 DEC 17 DGENE now includes more than 10 million sequences
NEWS 25 DEC 17 TOXCENTER enhanced with 2008 MeSH vocabulary in
           MEDLINE segment
NEWS 26 DEC 17 MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary
NEWS 27 DEC 17 CA/CAPplus enhanced with new custom IPC display formats
NEWS 28 DEC 17 STN Viewer enhanced with full-text patent content
           from USPATOLD
NEWS 29 JAN 02 STN pricing information for 2008 now available

NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2,
           CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
           AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

NEWS HOURS    STN Operating Hours Plus Help Desk Availability

```

NEWS LOGIN Welcome Banner and News Items
NEWS IPC8 For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 18:05:24 ON 15 JAN 2008

=> fil casreact

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
0.21	0.21

FULL ESTIMATED COST

FILE 'CASREACT' ENTERED AT 18:05:34 ON 15 JAN 2008

USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT

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Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications.

FILE CONTENT:1840 - 12 Jan 2008 VOL 148 ISS 3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

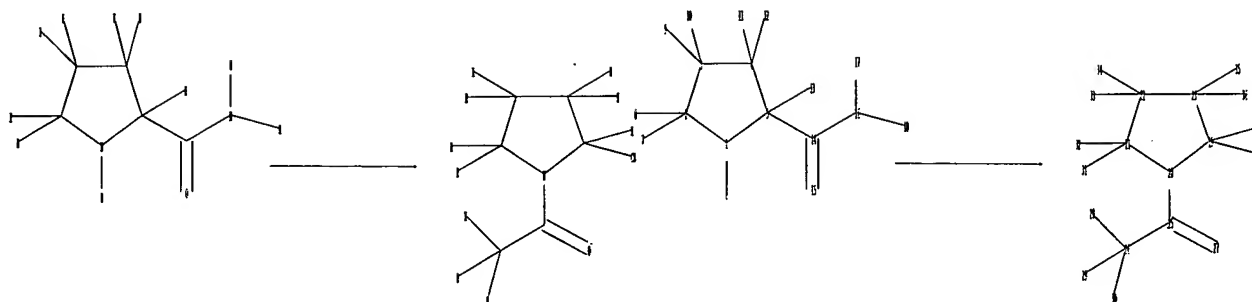
*
* CASREACT now has more than 13.8 million reactions *
*

Some CASREACT records are derived from the ZIC/VINITI database (1974-1999) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>

Uploading C:\Program Files\Stnexp\Queries\10552835\process1.str



```

chain nodes :
6 7 8 9 10 11 12 13 14 15 16 17 18 24 25 26 27 28 29 30 31 32
33 34 35 36 37
ring nodes :
1 2 3 4 5 19 20 21 22 23
chain bonds :
1-6 2-7 2-8 3-9 3-10 4-11 4-12 5-13 5-14 14-15 14-16 16-17 16-18 19-24
19-37 20-25 21-31 21-32 22-33 22-34 23-35 23-36 25-26 25-27 26-28 26-29
26-30
ring bonds :
1-2 1-5 2-3 3-4 4-5 19-20 19-23 20-21 21-22 22-23
exact/norm bonds :
1-2 1-5 2-3 3-4 4-5 14-15 14-16 19-20 19-23 20-21 20-25 21-22 22-23
25-27
exact bonds :
1-6 2-7 2-8 3-9 3-10 4-11 4-12 5-13 5-14 16-17 16-18 19-24 19-37 21-31
21-32 22-33 22-34 23-35 23-36 25-26 26-28 26-29 26-30

```

```

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS
10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS
18:CLASS 19:Atom 20:Atom 21:Atom 22:Atom 23:Atom 24:CLASS 25:CLASS 26:CLASS
27:CLASS 28:CLASS 29:CLASS 30:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS
35:CLASS 36:CLASS 37:CLASS
fragments assigned product role:
containing 19
fragments assigned reactant/reagent role:
containing 1
node mappings:
1:20 5:19 4:23 3:22 2:21

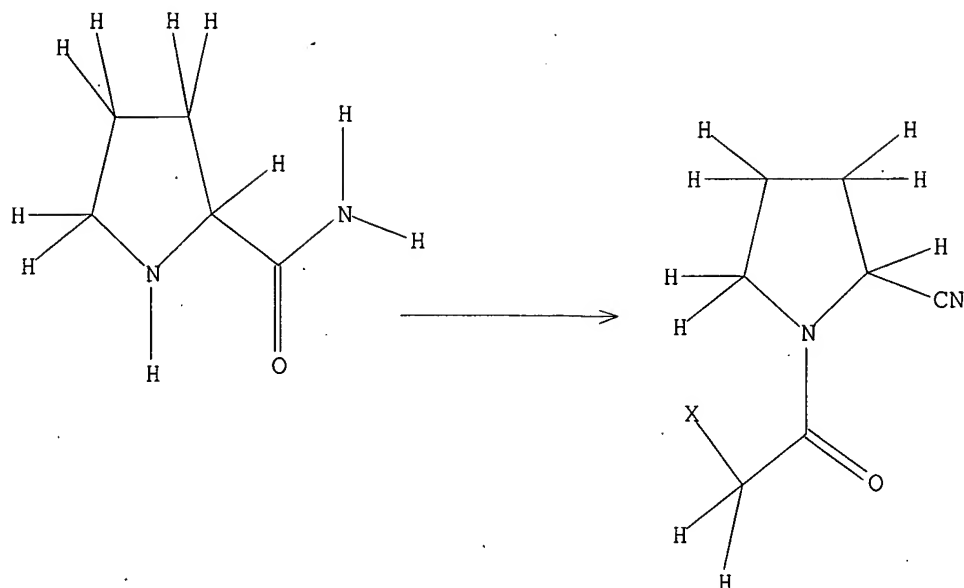
```

L1 STRUCTURE UPLOADED

=> d

L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s 11

SAMPLE SEARCH INITIATED 18:05:53 FILE 'CASREACT'

SCREENING COMPLETE - 2 REACTIONS TO VERIFY FROM 1 DOCUMENTS

100.0% DONE 2 VERIFIED 0 HIT RXNS 0 DOCS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED VERIFICATIONS: 2 TO 124

PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1 (0 REACTIONS)

=> s 11 full

FULL SEARCH INITIATED 18:05:57 FILE 'CASREACT'

SCREENING COMPLETE - 928 REACTIONS TO VERIFY FROM 31 DOCUMENTS

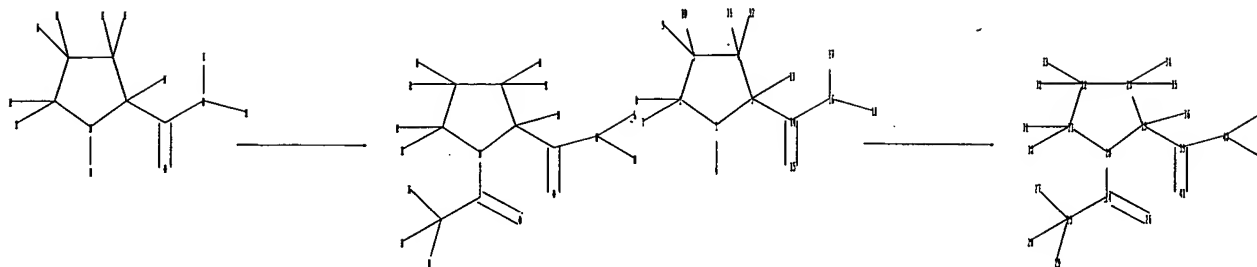
100.0% DONE 928 VERIFIED 7 HIT RXNS 4 DOCS

SEARCH TIME: 00.00.01

L3 4 SEA SSS FUL L1 (7 REACTIONS)

=>

Uploading C:\Program Files\Stnexp\Queries\10552835\process2.str



```

chain nodes :
6  7  8  9 10 11 12 13 14 15 16 17 18 24 25 26 27 28 29 30 31 32
33 34 35 36 39 40 41 42 43
ring nodes :
1  2  3  4  5 19 20 21 22 23
chain bonds :
1-6 2-7 2-8 3-9 3-10 4-11 4-12 5-13 5-14 14-15 14-16 16-17 16-18 19-36
19-39 20-24 21-30 21-31 22-32 22-33 23-34 23-35 24-25 24-26 25-27 25-28
25-29 39-40 39-41 40-42 40-43
ring bonds :
1-2 1-5 2-3 3-4 4-5 19-20 19-23 20-21 21-22 22-23
exact/norm bonds :
1-2 1-5 2-3 3-4 4-5 14-15 14-16 19-20 19-23 20-21 20-24 21-22 22-23
24-26 39-40 39-41
exact bonds :
1-6 2-7 2-8 3-9 3-10 4-11 4-12 5-13 5-14 16-17 16-18 19-36 19-39 21-30
21-31 22-32 22-33 23-34 23-35 24-25 25-27 25-28 25-29 40-42 40-43

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Match level :

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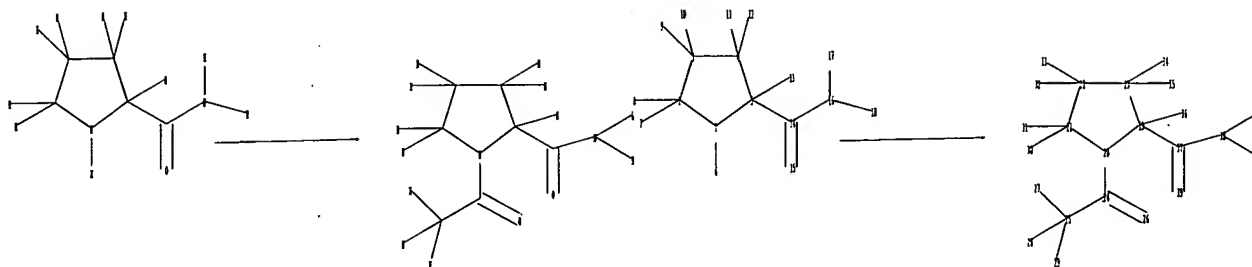
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS
10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS
18:CLASS 19:Atom 20:Atom 21:Atom 22:Atom 23:Atom 24:CLASS 25:CLASS 26:CLASS
27:CLASS 28:CLASS 29:CLASS 30:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS
35:CLASS 36:CLASS 39:CLASS 40:CLASS 41:CLASS 42:CLASS 43:CLASS

```

L4 STRUCTURE UPLOADED

=>

Uploading C:\Program Files\Stnexp\Queries\10552835\process3.str



```

chain nodes :
6  7  8  9 10 11 12 13 14 15 16 17 18 24 25 26 27 28 29 30 31 32
33 34 35 36 37 38 39 40 41
ring nodes :
1  2  3  4  5 19 20 21 22 23
chain bonds :
1-6 2-7 2-8 3-9 3-10 4-11 4-12 5-13 5-14 14-15 14-16 16-17 16-18 19-36
19-37 20-24 21-30 21-31 22-32 22-33 23-34 23-35 24-25 24-26 25-27 25-28
25-29 37-38 37-39 38-40 38-41
ring bonds :
1-2 1-5 2-3 3-4 4-5 19-20 19-23 20-21 21-22 22-23
exact/norm bonds :
1-2 1-5 2-3 3-4 4-5 14-15 14-16 19-20 19-23 20-21 20-24 21-22 22-23
24-26 37-38 37-39
exact bonds :
1-6 2-7 2-8 3-9 3-10 4-11 4-12 5-13 5-14 16-17 16-18 19-36 19-37 21-30
21-31 22-32 22-33 23-34 23-35 24-25 25-27 25-28 25-29 38-40 38-41

```

```

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS
10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS
18:CLASS 19:Atom 20:Atom 21:Atom 22:Atom 23:Atom 24:CLASS 25:CLASS 26:CLASS
27:CLASS 28:CLASS 29:CLASS 30:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS
35:CLASS 36:CLASS 37:CLASS 38:CLASS 39:CLASS 40:CLASS 41:CLASS
fragments assigned product role:
containing 19
fragments assigned reactant/reagent role:
containing 1
node mappings:
1:20 5:19 14:37 16:38 4:23 3:22 2:21

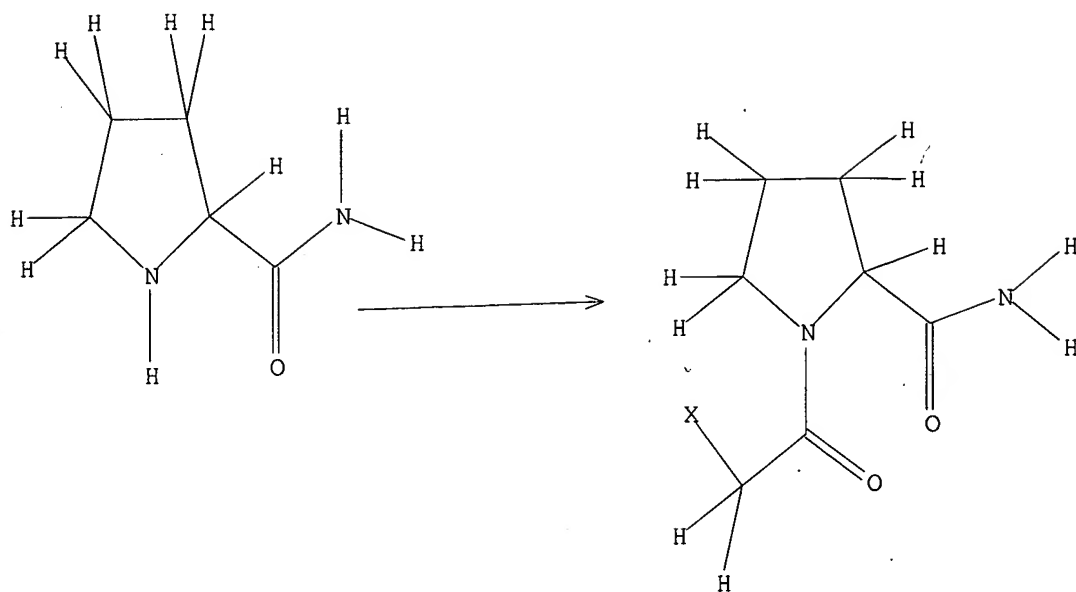
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L5 STRUCTURE UPLOADED

=> d

L5 HAS NO ANSWERS

L5 STR



Structure attributes must be viewed using STN Express query preparation.

=> s 15 full

FULL SEARCH INITIATED 18:07:51 FILE 'CASREACT'

SCREENING COMPLETE - 2979 REACTIONS TO VERIFY FROM

238 DOCUMENTS

100.0% DONE 2979 VERIFIED

7 HIT RXNS

6 DOCS

SEARCH TIME: 00.00.03

L6 6 SEA SSS FUL L5 (7 REACTIONS)

=> s 13 or 16

L7 7 L3 OR L6

=> s 17 and DMF

19823 DMF

L8 0 L7 AND DMF

=> d ibib abs hit L7 tot

L7 ANSWER 1 OF 7 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 145:471864 CASREACT
 TITLE: Preparation of multicyclic peptide derivatives as dipeptidyl peptidase-IV inhibitors
 INVENTOR(S): Kroth, Heiko; Feuerstein, Tim; Richter, Frank; Boer, Jürgen; Essers, Michael; Nolte, Bert; Schneider, Matthias; Hochguertel, Matthias; Frickel, Fritz-Frieder; Taveras, Arthur
 PATENT ASSIGNEE(S): Alantox Pharmaceuticals, Inc., USA
 SOURCE: PCT Int. Appl., 542pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

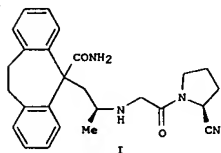
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006116157	A2	20061102	WO 2006-US15200	20060421
WO 2006116157	A9	20070301		
WO 2006116157	A3	20070419		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

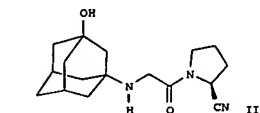
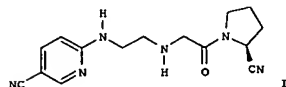
AU 2006239929 A1 20061102 AU 2006-239929 20060421
 CA 2599419 A1 20061102 CA 2006-2599419 20060421
 US 2006270701 A1 20061130 US 2006-409481 20060421
 IN 2007DN06747 A 20070921 IN 2007-DN6747 20070831
 US 2005-674151P 20050422
 WO 2006-US15200 20060421

PRIORITY APPL. INFO.:
 OTHER SOURCE(S): MARPAT 145:471864
 GI



L7 ANSWER 2 OF 7 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 139:133417 CASREACT
 TITLE: 1-[(3-Hydroxy-1-adamantyl)amino]acetyl-2-cyano-(S)-pyrrolidine: A Potent, Selective, and Orally Bioavailable Dipeptidyl Peptidase IV Inhibitor with Antihyperglycemic Properties
 AUTHOR(S): Villhauer, Edwin B.; Brinkman, John A.; Naderi, Goli B.; Burkey, Bryan F.; Dunning, Beth E.; Prasad, Kapa; Mangold, Bonnie L.; Russell, Mary E.; Hughes, Thomas E.
 CORPORATE SOURCE: Novartis Institute for Biomedical Research, East Hanover, NJ, 07936, USA
 SOURCE: Journal of Medicinal Chemistry (2003), 46(13), 2774-2789
 CODEN: JMCMAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



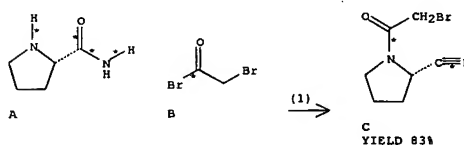
AB Dipeptidyl peptidase IV (DPP-IV) inhibition has the potential to become a valuable therapy for type 2 diabetes. The synthesis and structure-activity relationship of a new DPP-IV inhibitor class, N-substituted-glycyl-2-cyanopyrrolidines, are described as well as the path leading from the clin. development compound, 1-[2-[(5-cyanopyrrolidin-2-yl)amino]ethylamino]acetyl-2-cyano-(S)-pyrrolidine I (NVP-DPP728), to its follow-up, 1-[(3-hydroxy-1-adamantyl)amino]acetyl-2-cyano-(S)-pyrrolidine II (NVP-LAF237). The pharmacol. profile of II in obese Zucker fa/fa rats along with pharmacokinetic profile comparison of I and II in normal cynomolgus monkeys is discussed. The results suggest that II is a potent, stable, selective DPP-IV inhibitor possessing excellent oral bioavailability and potent antihyperglycemic activity with potential for once-a-day administration.

REFERENCE COUNT: 92 THERE ARE 92 CITED REFERENCES AVAILABLE FOR THIS

L7 ANSWER 1 OF 7 CASREACT COPYRIGHT 2008 ACS on STN (Continued)

AB The invention relates generally to pyrrolidine and thiazolidine DPP-IV inhibitory compds. A-B-CO-D (A is a bicyclic or tricyclic ring system attached to B at carbon or nitrogen; B is a linking group such as an amino acid residue or fragment; D is a pyrrolidine or thiazolidine residue or derivative), including isomers and pharmaceutically-acceptable salts, for treatment of DPP-IV mediated diseases, in particular, type-2 diabetes. Thus, pyrrolidinecarboxamide derivative I was prepared by reaction of 5-[(S)-2-aminopropyl]-10,11-dihydro-5H-dibenzo[a,d]cycloheptene-5-carboxamide with N-glyoxyloxy-L-prolinecarboxamide (prepn. given) and showed $K_i < 6$ nM for inhibition of DPP-IV.

RX(1) OF 627 A + B ==> C...



RX(1) RCT A 7531-52-4, B 598-21-0

STAGE(1)
 SOL 75-09-2 CH2Cl2
 CON room temperature

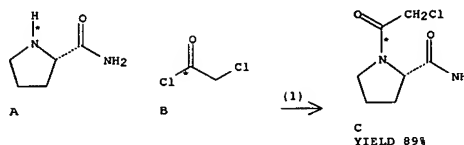
STAGE(2)
 RGT D 407-25-0 (CF3CO)2O
 SOL 75-09-2 CH2Cl2

PRO C 207557-33-3

L7 ANSWER 2 OF 7 CASREACT COPYRIGHT 2008 ACS on STN (Continued)

RECORD. ALL CITATIONS AVAILABLE IN THE RX
 FORMAT

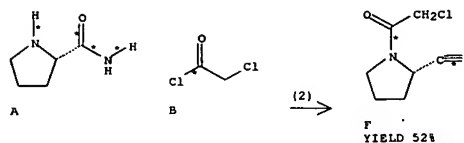
RX(1) OF 233 A + B ==> C...



RX(1) RCT A 7531-52-4, B 79-04-9

RGT D 584-08-7 K2CO3
 PRO C 214398-99-9
 SOL 109-99-9 THF
 CON SUBSTAGE(1) .5 hours, room temperature
 SUBSTAGE(2) 18 hours, room temperature

RX(2) OF 233 A + B ==> F...



RX(2) RCT A 7531-52-4, B 79-04-9

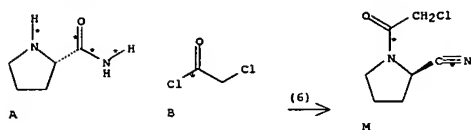
STAGE(1)
 RGT D 584-08-7 K2CO3
 SOL 109-99-9 THF
 CON SUBSTAGE(1) .75 hours, room temperature
 SUBSTAGE(2) 2 hours, room temperature

STAGE(2)
 RGT G 407-25-0 (CF3CO)2O
 CON 1 hour, room temperature

PRO F 207557-35-5

RX(6) OF 233 A + B ==> H...

L7 ANSWER 2 OF 7 CASREACT COPYRIGHT 2008 ACS on STN (Continued)



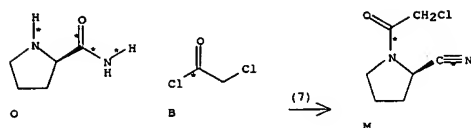
RX(6) RCT A 7531-52-4, B 79-04-9

STAGE(1)
RGT D 584-08-7 K2CO3
SOL 109-99-9 THF
CON 2 hours, room temperature

STAGE(2)
RGT G 407-25-0 (CF3CO)2O
CON 1 hour, room temperature

PRO M 565452-98-4

RX(7) OF 233 O + B ==> M...



RX(7) RCT O 62937-45-5, B 79-04-9

STAGE(1)
RGT D 584-08-7 K2CO3
SOL 109-99-9 THF
CON 2 hours, room temperature

STAGE(2)
RGT G 407-25-0 (CF3CO)2O
CON 1 hour, room temperature

PRO M 565452-98-4

L7 ANSWER 3 OF 7 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 139:69521 CASREACT
TITLE: Preparation of imidazolidineacetic acids and (imidazolidineacetyl)prolines for use in pharmaceutical synthesis
INVENTOR(S): Roe, Michael Bryan; Tartar, Andre
PATENT ASSIGNEE(S): Ferring BV, Neth.
SOURCE: PCT Int. Appl., 27 pp.
DOCUMENT TYPE: CODEN: PIXXD2
LANGUAGE: Patent
FAMILY ACC. NUM. COUNT: English
PATENT INFORMATION: 1

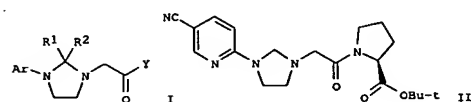
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003051848	A2	20030626	WO 2002-GB5631	20021212
WO 2003051848	A3	20030918		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002350942 A1 20030630 AU 2002-350942 20021212
GB 2001-29988 20011214
WO 2002-GB5631 20021212

PRIORITY APPLN. INFO.:
OTHER SOURCE(S): MARPAT 139:69521
GI

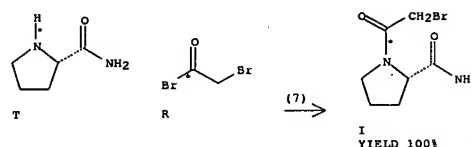


AB Title compds. I [wherein Ar = (un)substituted Ph or heteroaryl; R1 and R2 = independently H or alkyl, preferably H, Me, or Et; X = OH, alkoxy, aralkoxy, O-resin, NH2, alkylamino, aralkylamino, or NH-resin; Y = OH, alkoxy, aralkoxy, 2-cyano-1-pyrrolidinyl, prolinyl, or prolinamido] were prepared by the reaction of an N-arylimidazolidine with an acetic acid derivative. I are useful in the synthesis of pharmaceutically active ethylenediamine derivs. Synthesis of title imidazolidines is more selective and provides higher yields than alkylation of the corresponding ethylenediamine derivs. For example, reaction of 6-chloronicotinonitrile and tert-Bu (2-aminoethyl)carbamate gave tert-Bu [2-(5-cyano-2-pyridylamino)ethyl]carbamate (65%). Deprotection with trifluoroacetic acid provided the amine salt (100%), which was cyclized with HCHO to afford the imidazoline (33%). Alkylation of the imidazoline with N-bromoacetyl-L-proline tert-Bu ester using TEA in THF gave II (35%).

L7 ANSWER 2 OF 7 CASREACT COPYRIGHT 2008 ACS on STN (Continued)

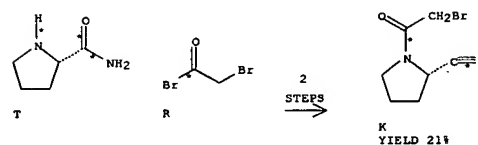
L7 ANSWER 3 OF 7 CASREACT COPYRIGHT 2008 ACS on STN (Continued)

RX(7) OF 60 T + R ==> I...



RX(7) RCT T 7531-52-4, R 598-21-0
RGT G 121-44-8 Et3N, S 1122-58-3 4-DMAP
PRO I 253309-37-4
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 1 hour
SUBSTAGE(2) 2 hours

RX(19) OF 60 COMPOSED OF RX(7), RX(8)
RX(19) T + R ==> K



RX(7) RCT T 7531-52-4, R 598-21-0
RGT G 121-44-8 Et3N, S 1122-58-3 4-DMAP
PRO I 253309-37-4
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 1 hour
SUBSTAGE(2) 2 hours

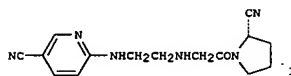
RX(8) RCT I 253309-37-4

STAGE(1)
RGT U 407-25-0 (CF3CO)2O
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) room temperature -> 0 deg C
SUBSTAGE(2) 15 minutes, 0 deg C
SUBSTAGE(3) 2 hours

STAGE(2)
RGT M 144-55-8 NaHCO3

L7 ANSWER 3 OF 7 CASREACT COPYRIGHT 2008 ACS on STN (Continued)
 SOL 7732-18-5 Water
 CON 0 deg C
 PRO K 207557-33-3

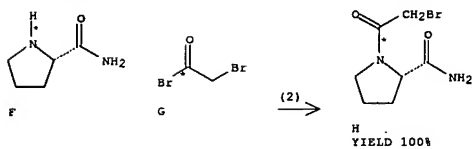
L7 ANSWER 4 OF 7 CASREACT COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 137:78828 CASREACT
 TITLE: 1-[2-[(5-Cyanopyridin-2-yl)amino]ethylamino]acetyl-2-(8)-pyrrolidinecarbonitrile: A Potent, Selective, and Orally Bioavailable Dipeptidyl Peptidase IV Inhibitor with Antihyperglycemic Properties
 AUTHOR(S): Villhauer, Edwin B.; Brinkman, John A.; Naderi, Goli B.; Dunning, Beth E.; Mangold, Bonnie L.; Mone, Manisha D.; Russell, Mary E.; Weldon, Stephen C.; Hughes, Thomas E.
 CORPORATE SOURCE: Novartis Institute for Biomedical Research, Summit, NJ, 07901, USA
 SOURCE: Journal of Medicinal Chemistry (2002), 45(12), 2362-2365
 CODEN: JMCMAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



AB Dipeptidyl peptidase IV (DPP-IV) inhibition has the potential to become a valuable therapy for type 2 diabetes. We report the first use of solid-phase synthesis in the discovery of a new DPP-IV inhibitor class and a solution-phase synthesis that is practical up to the multikilogram scale.
 One compound, NVP-DPP728 (I), is profiled as a potent, selective, and short-acting DPP-IV inhibitor that has excellent oral bioavailability and potent antihyperglycemic activity.
 REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

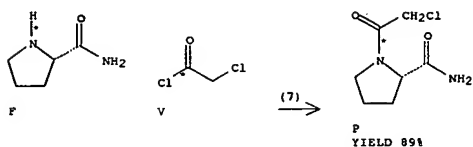
RX(2) OF 36 F + G ==> H...

L7 ANSWER 4 OF 7 CASREACT COPYRIGHT 2008 ACS on STN (Continued)



RX(2) RCT F 7531-52-4
 STAGE(1)
 RGT I 121-44-8 Et3N, J 1122-58-3 4-DMAP
 SOL 75-09-2 CH2Cl2
 STAGE(2)
 RCT G 598-21-0
 SOL 75-09-2 CH2Cl2
 STAGE(3)
 SOL 141-78-6 AcOEt
 PRO H 253309-37-4
 NTE stereoselective

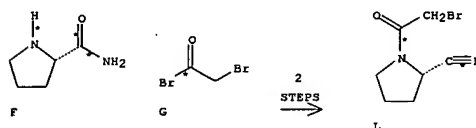
RX(7) OF 36 F + V ==> P...



RX(7) RCT F 7531-52-4
 STAGE(1)
 SOL 109-99-9 THF
 STAGE(2)
 RCT V 79-04-9
 RGT W 584-08-7 K2CO3
 SOL 109-99-9 THF
 PRO P 214398-99-9
 NTE stereoselective

L7 ANSWER 4 OF 7 CASREACT COPYRIGHT 2008 ACS on STN (Continued)

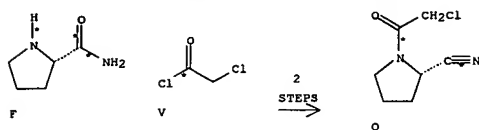
RX(13) OF 36 COMPOSED OF RX(2), RX(3)
 RX(13) F + G ==> L



RX(2) RCT F 7531-52-4
 STAGE(1)
 RGT I 121-44-8 Et3N, J 1122-58-3 4-DMAP
 SOL 75-09-2 CH2Cl2
 STAGE(2)
 RCT G 598-21-0
 SOL 75-09-2 CH2Cl2
 STAGE(3)
 SOL 141-78-6 AcOEt
 PRO H 253309-37-4
 NTE stereoselective
 RX(3) RCT H 253309-37-4
 STAGE(1)
 SOL 75-09-2 CH2Cl2
 STAGE(2)
 RGT M 407-25-0 (CF3CO)2O
 STAGE(3)
 RGT N 144-55-8 NaHCO3
 SOL 7732-18-5 Water, 141-78-6 AcOEt
 PRO L 207557-33-3
 NTE stereoselective

RX(18) OF 36 COMPOSED OF RX(7), RX(4)
 RX(18) F + V ==> Q

L7 ANSWER 4 OF 7 CASREACT COPYRIGHT 2008 ACS on STN (Continued)



RX(7) RCT F 7531-52-4

STAGE(1)
SOL 109-99-9 THFSTAGE(2)
RCT V 79-04-9
RGT W 584-08-7 K2CO3
SOL 109-99-9 THFPRO P 214398-99-9
NTE stereoselective

RX(4) RCT P 214398-99-9

STAGE(1)
SOL 75-09-2 CH2Cl2STAGE(2)
RGT M 407-25-0 (CF3CO)2OSTAGE(3)
RGT N 144-55-8 NaHCO3
SOL 7732-18-5 Water, 75-09-2 CH2Cl2

PRO Q 207557-35-5

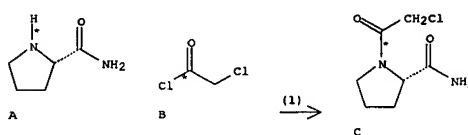
L7 ANSWER 5 OF 7 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 134:251952 CASREACT
 TITLE: Methods for the acylation of amine compounds
 INVENTOR(S): Fitt, John Joseph, Sr.; Kapa, Prasad Koteswara
 PATENT ASSIGNEE(S): Novartis Pharmaceuticals Corp., USA
 SOURCE: U.S., 4 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6211384	B1	20010403	US 1999-385722	19990830

PRIORITY APPLN. INFO.: MARPAT 134:251952
 OTHER SOURCE(S):
 AB Amines were acylated by reacting a first reactant containing an amine group with a second reactant containing an acyl halide group. The reaction takes place in the presence of secondary carboxylic acid salt forms, of formula R4R5CHCO2H (R4 is an alkyl group having 1 to 10 carbon atoms; R5 is an alkyl group having 1 to 10 carbon atoms). E.g., chloroacetyl chloride was added to L-prolinamide and sodium 2-ethylhexanoate in t-Bu Me ether to give the acylated L-prolinamide.
 REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

RX(1) OF 6 A + B ----> C



RX(1) RCT A 7531-52-4

STAGE(1)
RGT D 19766-89-3 Na 2-ethylhexanoate
SOL 1634-04-4 t-BuOMeSTAGE(2)
RCT B 79-04-9
RGT E 149-57-5 2-Ethylhexanoic acid

L7 ANSWER 5 OF 7 CASREACT COPYRIGHT 2008 ACS on STN (Continued)

PRO C 214398-99-9

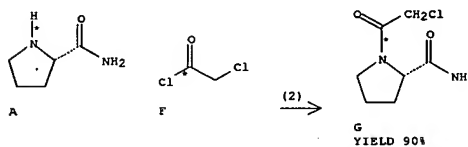
L7 ANSWER 6 OF 7 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 129:302823 CASREACT
 TITLE: Sodium 2-ethylhexanoate: a mild acid scavenger useful in acylation of amines
 AUTHOR(S): Fitt, John; Prasad, Kapa; Repic, Oljan; Blacklock, Thomas J.
 CORPORATE SOURCE: Process R&D, Chem. Anal. Dev., Novartis Pharm. Corp., East Hanover, NJ, 07936, USA
 SOURCE: Tetrahedron Letters (1998), 39(39), 6991-6992
 CODEN: TELEAY; ISSN: 0040-4039
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB A highly useful method for the acylation of amines with acid chlorides utilizing sodium 2-ethylhexanoate as the base is described. This procedure is superior to the Schotten-Baumann conditions whenever the product is water soluble

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

RX(2) OF 6 A + F ----> G

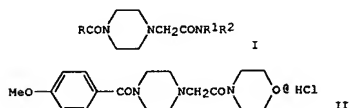


RX(2) RCT A 7531-52-4, F 79-04-9
 RGT D 19766-89-3 Na 2-ethylhexanoate
 PRO G 214398-99-9
 SOL 109-99-9 THF

L7 ANSWER 7 OF 7 CASREACT COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 102:95674 CASREACT
 TITLE: Substituted piperazin-1-yl-acetic-acid amides, and their use
 INVENTOR(S): Schoenafinger, Karl; Beyerle, Rudi; Schindler, Ursula;
 PATENT ASSIGNEE(S): Martorane, Piero; Nitz, Rolf Eberhard
 SOURCE: Cassella A.-G., Fed. Rep. Ger. Eur. Pat. Appl., 32 pp.
 DOCUMENT TYPE: CODEN: EPXXDW
 LANGUAGE: Patent
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION: German

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 123977	A1	19841107	EP 1984-104042	19840411
DE 3315424	A1	19841220	DE 1983-3315424	19830428
DK 8401477	A	19841029	DK 1984-1477	19840229
FI 8401461	A	19841029	FI 1984-1461	19840412
NO 8401464	A	19841029	NO 1984-1464	19840412
US 4610984	A	19860909	US 1984-601637	19840418
JP 59205363	A	19841120	JP 1984-80360	19840423
DD 223711	A5	19850619	DD 1984-262312	19840425
CS 244811	B2	19860814	CS 1984-3071	19840425
HU 34178	A2	19850228	HU 1984-1608	19840426
AU 8427473	A	19841101	AU 1984-27473	19840427
ZA 8403138	A	19841128	ZA 1984-3138	19840427
CA 1202304	A1	19860325	CA 1984-452963	19840427
CS 244849	B2	19860814	CS 1985-1217	19850220
PRIORITY APPLN. INFO.:			DE 1983-3315424	19830428
			CS 1984-3071	19840425

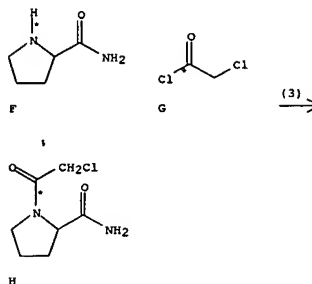
OTHER SOURCE(S): MARPAT 102:95674
 GI



AB The title compds. [I: R = amino, ClC6H4OCH2, pyridinyl, thienyl, furanyl, (un)substituted Ph; R1, R2 = H, (un)substituted alkyl; R1R2 = cyclohexylmethylene; NR1R2 = morpholino, piperidino, 1-pyrrolidinyl, 4-methyl-1-piperazinyl] were prepared Thus, 10.25 g 4-(1-piperazinylacetyl)morpholine was acylated with 4-MeOC6H4COCl to give 14.6

L7 ANSWER 7 OF 7 CASREACT COPYRIGHT 2008 ACS on STN (Continued)
 g II. II enhanced learning and memory in mice in the passive avoidance test with a min. ED of 3 mg/kg orally.

RX(3) OF 6 F + G ==> H...

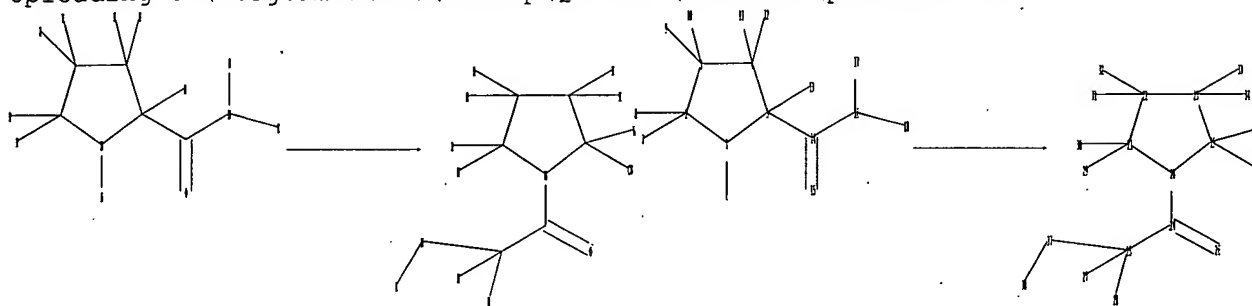


RX(3) RCT F 2812-47-7, G 79-04-9
 PRO H 94747-48-5

X

=>

Uploading C:\Program Files\Stnexp\Queries\10552835\process4.str



chain nodes :

6 7 8 9 10 11 12 13 14 15 16 17 18 24 25 26 27 28 29 30 31 32
33 34 35 36 37 38

ring nodes :

1 2 3 4 5 19 20 21 22 23

chain bonds :

1-6 2-7 2-8 3-9 3-10 4-11 4-12 5-13 5-14 14-15 14-16 16-17 16-18 19-35
19-36 20-24 21-29 21-30 22-31 22-32 23-33 23-34 24-25 24-26 25-28 25-27
25-37 37-38

ring bonds :

1-2 1-5 2-3 3-4 4-5 19-20 19-23 20-21 21-22 22-23

exact/norm bonds :

1-2 1-5 2-3 3-4 4-5 14-15 14-16 19-20 19-23 20-21 20-24 21-22 22-23
24-26 25-37

exact bonds :

1-6 2-7 2-8 3-9 3-10 4-11 4-12 5-13 5-14 16-17 16-18 19-35 19-36 21-29
21-30 22-31 22-32 23-33 23-34 24-25 25-28 25-27 37-38

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS
10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS
18:CLASS 19:Atom 20:Atom 21:Atom 22:Atom 23:Atom 24:CLASS 25:CLASS 26:CLASS
27:CLASS 28:CLASS 29:CLASS 30:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS
35:CLASS 36:CLASS 37:CLASS 38:CLASS

fragments assigned product role:

containing 19

fragments assigned reactant/reagent role:

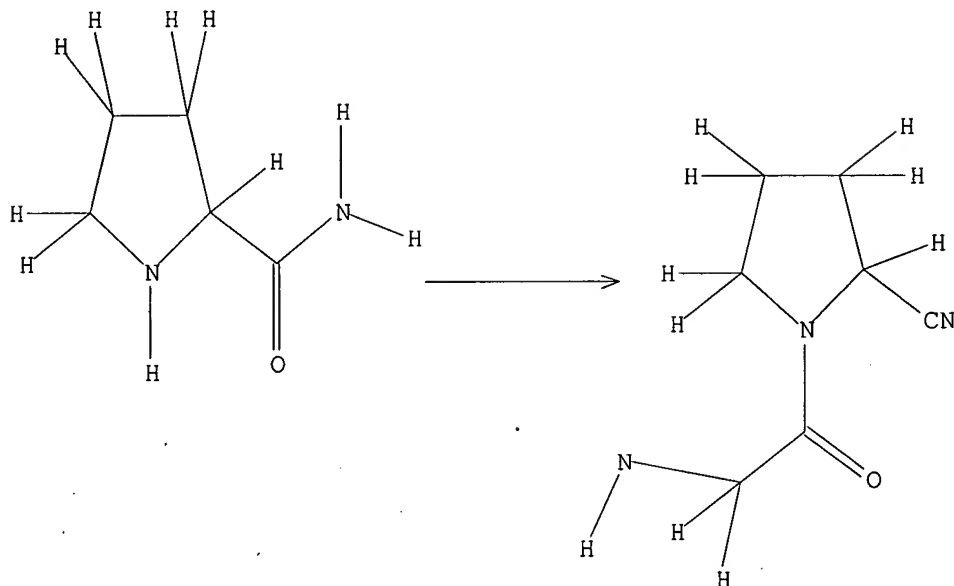
containing 1

node mappings:

1:20 5:19 4:23 3:22 2:21

L9 STRUCTURE UPLOADED

=> d
 L9 HAS NO ANSWERS
 L9 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l9 full
 FULL SEARCH INITIATED 18:13:44 FILE 'CASREACT'
 SCREENING COMPLETE - 1744 REACTIONS TO VERIFY FROM 47 DOCUMENTS
 100.0% DONE 1744 VERIFIED 219 HIT RXNS 6 DOCS
 SEARCH TIME: 00.00.01

L10 6 SEA SSS FUL L9 (219 REACTIONS)

=> d his

(FILE 'HOME' ENTERED AT 18:05:24 ON 15 JAN 2008)

FILE 'CASREACT' ENTERED AT 18:05:34 ON 15 JAN 2008

L1 STRUCTURE UPLOADED
 L2 0 S L1
 L3 4 S L1 FULL
 L4 STRUCTURE UPLOADED
 L5 STRUCTURE UPLOADED
 L6 6 S L5 FULL
 L7 7 S L3 OR L6
 L8 0 S L7 AND DMF
 L9 STRUCTURE UPLOADED
 L10 6 S L9 FULL

=> s 110 or 17
L11 9 L10 OR L7

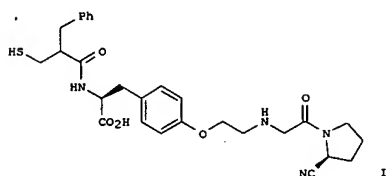
=> s 110 not 17
L12 2 L10 NOT L7

=> d ibib abs hit 112 tot

L12 ANSWER 1 OF 2 CASREACT COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 144:254389 CASREACT
 TITLE: Preparation of novel peptidomimetics for inhibition
 of dipeptidyl peptidase (DPP-IV) and neprilysin (NEP)
 and/or angiotensin converting enzyme (ACE)
 INVENTOR(S): Pierau, Sabine; Oefner, Christian; Dale, Glenn E.
 PATENT ASSIGNEE(S): Morphochem AG, Germany
 SOURCE: U.S. Pat. Appl., 17 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006046978	A1	20060302	US 2004-930606	20040831
PRIORITY APPL. INFO.:			US 2004-930606	20040831

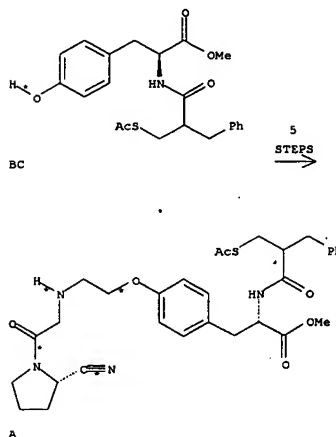
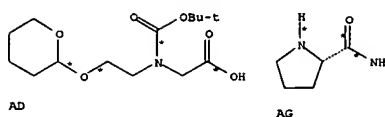
GI



AB The invention relates to novel compds. of general formula A-L-B, A-L-C and A-L-D, where A is an inhibitor of DPP-IV, B is an inhibitor of neprilysin, C is an inhibitor of ACE, D is an inhibitor of vasopeptidases (especially NEP and ACE) (or pharmacophores of A, B, C or D) and L is a linker, or a pharmaceutically-acceptable salt, solvent, or formulation, which are useful for the treatment as well as the prevention of type 2 diabetes mellitus. Thus, peptidomimetic compound I was prepared by a multistep procedure which includes reactions of L-prolinamide and L-tyrosine Me ester.

RX(249) OF 361 COMPOSED OF RX(12), RX(13), RX(14), RX(19), RX(20)
 RX(249) AD + AG + BC ==> A

L12 ANSWER 1 OF 2 CASREACT COPYRIGHT 2008 ACS on STN (Continued)



RX(12) RCT AD 752218-12-5, AG 7531-52-4
 RGT AI 538-75-0 DCC, AJ 2592-95-2 1-Benzotriazolol, AK 109-02-4
 N-Methylmorpholine
 PRO AH 877373-92-7
 SOL 75-09-2 CH2Cl2
 CON 24 hours, room temperature
 RX(13) RCT AH 877373-92-7

L12 ANSWER 1 OF 2 CASREACT COPYRIGHT 2008 ACS on STN (Continued)

STAGE(1)
 RGT AM 288-32-4 1H-Imidazole
 SOL 110-86-1 Pyridine
 CON SUBSTAGE(1) room temperature
 SUBSTAGE(2) room temperature -> -5 deg C

STAGE(2)
 RGT AN 10025-87-3 POC13
 CON SUBSTAGE(1) -5 deg C
 SUBSTAGE(2) -5 deg C -> room temperature

PRO AL 752218-16-9

RX(14) RCT AL 752218-16-9
 RGT AQ 24057-28-1 Pyridinium tosylate
 PRO AP 752218-18-1
 SOL 64-17-5 EtOH
 CON 6 hours, 60 deg C

RX(19) RCT AP 752218-18-1

STAGE(1)
 RGT BH 603-35-0 PPh3, BI 1972-28-7 EtO2CN:NCO2Et
 SOL 109-99-9 THF
 CON 1 hour, room temperature

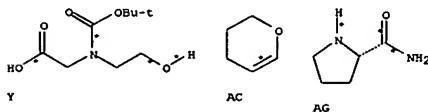
STAGE(2)
 RCT BC 124735-31-5
 CON 2 days, room temperature

STAGE(3)
 RGT BH 603-35-0 PPh3, BI 1972-28-7 EtO2CN:NCO2Et
 CON 24 hours, room temperature

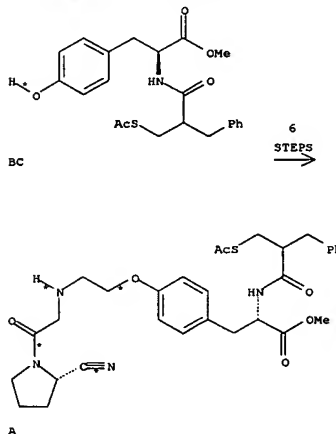
PRO BG 752218-25-0

RX(20) RCT BG 752218-25-0
 RGT F 76-05-1 F3CCO2H
 PRO A 752218-27-2
 SOL 7732-18-5 Water
 CON 3 hours, room temperature

RX(250) OF 361 COMPOSED OF RX(11), RX(12), RX(13), RX(14), RX(19), RX(20)
 RX(250) Y + AC + AG + BC ==> A



L12 ANSWER 1 OF 2 CASREACT COPYRIGHT 2008 ACS on STN (Continued)



RX(11) RCT Y 189160-67-6, AC 110-87-2
 RGT AE 9037-24-5 Amberlyst 15
 PRO AD 752218-12-5
 SOL 75-09-2 CH2Cl2
 CON 24 hours, room temperature
 RX(12) RCT AD 752218-12-5, AG 7531-52-4
 RGT AI 538-75-0 DCC, AJ 2592-95-2 1-Benzotriazolol, AK 109-02-4
 N-Methylmorpholine
 PRO AH 877373-92-7
 SOL 75-09-2 CH2Cl2
 CON 24 hours, room temperature
 RX(13) RCT AH 877373-92-7

STAGE(1)
 RGT AM 288-32-4 1H-Imidazole
 SOL 110-86-1 Pyridine
 CON SUBSTAGE(1) room temperature
 SUBSTAGE(2) room temperature -> -5 deg C

STAGE(2)
 RGT AN 10025-87-3 POC13
 CON SUBSTAGE(1) -5 deg C
 SUBSTAGE(2) -5 deg C -> room temperature

L12 ANSWER 1 OF 2 CASREACT COPYRIGHT 2008 ACS on STN (Continued)

PRO AL 752218-16-9

RX(14) RCT AL 752218-16-9
 RGT AQ 24057-28-1 Pyridinium tosylate
 PRO AP 752218-18-1
 SOL 64-17-5 EtOH
 CON 6 hours, 60 deg C

RX(19) RCT AP 752218-18-1

STAGE(1)
 RGT BH 603-35-0 PPh3, BI 1972-28-7 EtO2CN:NCO2Et
 SOL 109-99-9 THF
 CON 1 hour, room temperature

STAGE(2)
 RCT BC 124735-31-5
 CON 2 days, room temperature

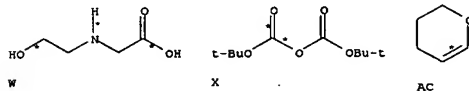
STAGE(3)
 RGT BH 603-35-0 PPh3, BI 1972-28-7 EtO2CN:NCO2Et
 CON 24 hours, room temperature

PRO BG 752218-25-0

RX(20) RCT BG 752218-25-0
 RGT F 76-05-1 F3CCO2H
 PRO A 752218-27-2
 SOL 7732-18-5 Water
 CON 3 hours, room temperature

RX(251) OF 361 COMPOSED OF RX(10), RX(11), RX(12), RX(13), RX(14), RX(19),
 RX(20)

RX(251) W + X + AC + AG + BC ==> A



L12 ANSWER 1 OF 2 CASREACT COPYRIGHT 2008 ACS on STN (Continued)

RCT AI 538-75-0 DCC, AJ 2592-95-2 1-Benzotriazolol, AK 109-02-4
 N-Methylmorpholine
 PRO AH 877373-92-7
 SOL 75-09-2 CH2Cl2
 CON 24 hours, room temperature

RX(13) RCT AH 877373-92-7

STAGE(1)
 RGT AM 288-32-4 1H-Imidazole
 SOL 110-86-1 Pyridine
 CON SUBSTAGE(1) room temperature
 SUBSTAGE(2) room temperature -> -5 deg C

STAGE(2)
 RGT AN 10025-87-3 POCl3
 CON SUBSTAGE(1) -5 deg C
 SUBSTAGE(2) -5 deg C -> room temperature

PRO AL 752218-16-9

RX(14) RCT AL 752218-16-9
 RGT AQ 24057-28-1 Pyridinium tosylate
 PRO AP 752218-18-1
 SOL 64-17-5 EtOH
 CON 6 hours, 60 deg C

RX(19) RCT AP 752218-18-1

STAGE(1)
 RGT BH 603-35-0 PPh3, BI 1972-28-7 EtO2CN:NCO2Et
 SOL 109-99-9 THF
 CON 1 hour, room temperature

STAGE(2)
 RCT BC 124735-31-5
 CON 2 days, room temperature

STAGE(3)
 RGT BH 603-35-0 PPh3, BI 1972-28-7 EtO2CN:NCO2Et
 CON 24 hours, room temperature

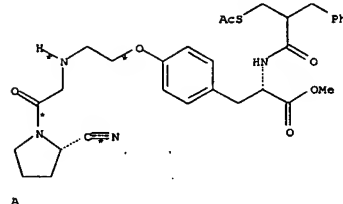
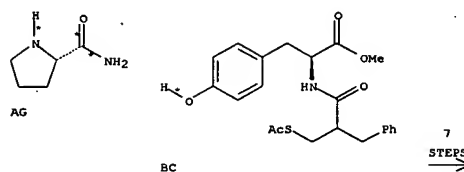
PRO BG 752218-25-0

RX(20) RCT BG 752218-25-0
 RGT F 76-05-1 F3CCO2H
 PRO A 752218-27-2
 SOL 7732-18-5 Water
 CON 3 hours, room temperature

RX(252) OF 361 COMPOSED OF RX(9), RX(10), RX(11), RX(12), RX(13), RX(14),
 RX(19), RX(20)

RX(252) U + V + X + AC + AG + BC ==> A

L12 ANSWER 1 OF 2 CASREACT COPYRIGHT 2008 ACS on STN (Continued)



RX(10) RCT W 5835-28-9, X 24424-99-5

STAGE(1)
 RGT Z 1310-73-2 NaOH
 SOL 7732-18-5 Water, 123-91-1 Dioxane
 CON 24 hours, room temperature

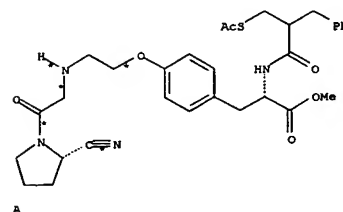
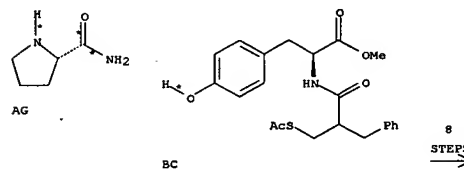
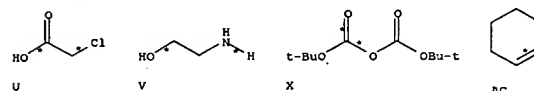
STAGE(2)
 RGT AA 7647-01-0 HCl
 SOL 7732-18-5 Water

PRO Y 189160-67-6

RX(11) RCT Y 189160-67-6, AC 110-87-2
 RGT AE 9037-24-5 Amberlyst 15
 PRO AD 752218-12-5
 SOL 75-09-2 CH2Cl2
 CON 24 hours, room temperature

RX(12) RCT AD 752218-12-5, AG 7531-52-4

L12 ANSWER 1 OF 2 CASREACT COPYRIGHT 2008 ACS on STN (Continued)



RX(9) RCT U 79-11-8, V 141-43-5
 PRO W 5835-28-9
 SOL 7732-18-5 Water
 CON 24 hours, room temperature

RX(10) RCT W 5835-28-9, X 24424-99-5

STAGE(1)
 RGT Z 1310-73-2 NaOH
 SOL 7732-18-5 Water, 123-91-1 Dioxane
 CON 24 hours, room temperature

STAGE(2)
 RGT AA 7647-01-0 HCl

L12 ANSWER 1 OF 2 CASREACT COPYRIGHT 2008 ACS on STN (Continued)
SOL 7732-18-5 Water

PRO Y 189160-67-6

RX(11) RCT Y 189160-67-6, AC 110-87-2
RGT AE 9037-24-5 Amberlyst 15
PRO AD 752218-12-5
SOL 75-09-2 CH₂Cl₂
CON 24 hours, room temperature

RX(12) RCT AD 752218-12-5, AG 7531-52-4
RGT AI 538-75-0 DCC, AJ 2592-95-2 1-Benzotriazolol, AK 109-02-4
N-Methylmorpholine
PRO AH 877373-92-7
SOL 75-09-2 CH₂Cl₂
CON 24 hours, room temperature

RX(13) RCT AH 877373-92-7

STAGE(1)

RGT AM 288-32-4 1H-Imidazole
SOL 110-86-1 Pyridine
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> -5 deg C

STAGE(2)

RGT AN 10025-87-3 POC13
CON SUBSTAGE(1) -5 deg C
SUBSTAGE(2) -5 deg C -> room temperature

PRO AL 752218-16-9

RX(14) RCT AL 752218-16-9
RGT AQ 24057-28-1 Pyridinium tosylate
PRO AP 752218-18-1
SOL 64-17-5 EtOH
CON 6 hours, 60 deg C

RX(19) RCT AP 752218-18-1

STAGE(1)

RGT BH 603-35-0 PPh₃, BI 1972-28-7 EtO₂CN:CO₂Et
SOL 109-99-9 THF
CON 1 hour, room temperature

STAGE(2)

RCT BC 124735-31-5
CON 2 days, room temperature

STAGE(3)

RGT BH 603-35-0 PPh₃, BI 1972-28-7 EtO₂CN:CO₂Et
CON 24 hours, room temperature

PRO BG 752218-25-0

L12 ANSWER 1 OF 2 CASREACT COPYRIGHT 2008 ACS on STN (Continued)

RX(12) RCT AD 752218-12-5, AG 7531-52-4
RGT AI 538-75-0 DCC, AJ 2592-95-2 1-Benzotriazolol, AK 109-02-4
N-Methylmorpholine
PRO AH 877373-92-7
SOL 75-09-2 CH₂Cl₂
CON 24 hours, room temperature

RX(13) RCT AH 877373-92-7

STAGE(1)

RGT AM 288-32-4 1H-Imidazole
SOL 110-86-1 Pyridine
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> -5 deg C

STAGE(2)

RGT AN 10025-87-3 POC13
CON SUBSTAGE(1) -5 deg C
SUBSTAGE(2) -5 deg C -> room temperature

PRO AL 752218-16-9

RX(14) RCT AL 752218-16-9
RGT AQ 24057-28-1 Pyridinium tosylate
PRO AP 752218-18-1
SOL 64-17-5 EtOH
CON 6 hours, 60 deg C

RX(19) RCT AP 752218-18-1

STAGE(1)

RGT BH 603-35-0 PPh₃, BI 1972-28-7 EtO₂CN:CO₂Et
SOL 109-99-9 THF
CON 1 hour, room temperature

STAGE(2)

RCT BC 124735-31-5
CON 2 days, room temperature

STAGE(3)

RGT BH 603-35-0 PPh₃, BI 1972-28-7 EtO₂CN:CO₂Et
CON 24 hours, room temperature

PRO BG 752218-25-0

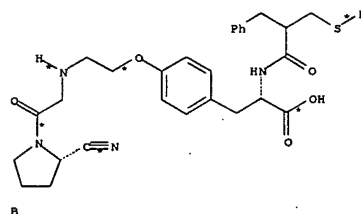
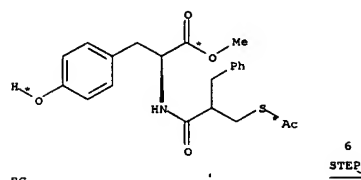
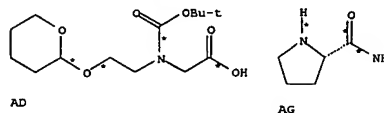
RX(20) RCT BG 752218-25-0
RGT F 76-05-1 F₃CCO₂H
PRO A 752218-27-2
SOL 7732-18-5 Water
CON 3 hours, room temperature

RX(1) RCT A 752218-27-2
RGT C 1310-65-2 LiOH
PRO B 752218-29-4
SOL 109-99-9 THF
CON 24 hours, room temperature

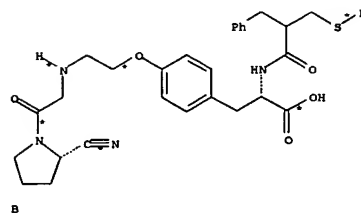
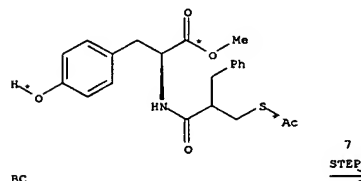
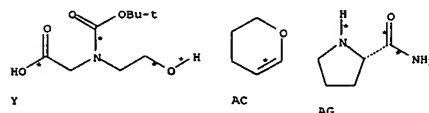
L12 ANSWER 1 OF 2 CASREACT COPYRIGHT 2008 ACS on STN (Continued)

RX(20) RCT BG 752218-25-0
RGT F 76-05-1 F₃CCO₂H
PRO A 752218-27-2
SOL 7732-18-5 Water
CON 3 hours, room temperature

RX(254) OF 361 COMPOSED OF RX(12), RX(13), RX(14), RX(19), RX(20), RX(1)
RX(254) AD + AG + BC -> B



L12 ANSWER 1 OF 2 CASREACT COPYRIGHT 2008 ACS on STN (Continued)
RX(255) OF 361 COMPOSED OF RX(11), RX(12), RX(13), RX(14), RX(19), RX(20),
RX(1)
RX(255) Y + AC + AG + BC -> B



RX(11) RCT Y 189160-67-6, AC 110-87-2
RGT AE 9037-24-5 Amberlyst 15
PRO AD 752218-12-5
SOL 75-09-2 CH₂Cl₂
CON 24 hours, room temperature

RX(12) RCT AD 752218-12-5, AG 7531-52-4
RGT AI 538-75-0 DCC, AJ 2592-95-2 1-Benzotriazolol, AK 109-02-4

L12 ANSWER 1 OF 2 CASREACT COPYRIGHT 2008 ACS on STN (Continued)

N-Methylmorpholine
 PRO AH 877373-92-7
 SOL 75-09-2 CH2Cl2
 CON 24 hours, room temperature

RX(13) RCT AH 877373-92-7

STAGE(1)
 RGT AM 288-32-4 1H-Imidazole
 SOL 110-86-1 Pyridine
 CON SUBSTAGE(1) room temperature
 SUBSTAGE(2) room temperature -> -5 deg C

STAGE(2)
 RGT AN 10025-87-3 POC13
 CON SUBSTAGE(1) -5 deg C
 SUBSTAGE(2) -5 deg C -> room temperature

PRO AL 752218-16-9

RX(14) RCT AL 752218-16-9
 RGT AQ 24057-28-1 Pyridinium tosylate
 PRO AP 752218-18-1
 SOL 64-17-5 EtOH
 CON 6 hours, 60 deg C

RX(19) RCT AP 752218-18-1

STAGE(1)
 RGT BH 603-35-0 PPh3, BI 1972-28-7 EtO2CN:NCO2Et
 SOL 109-99-9 THF
 CON 1 hour, room temperature

STAGE(2)
 RCT BC 124735-31-5
 CON 2 days, room temperature

STAGE(3)
 RGT BH 603-35-0 PPh3, BI 1972-28-7 EtO2CN:NCO2Et
 CON 24 hours, room temperature

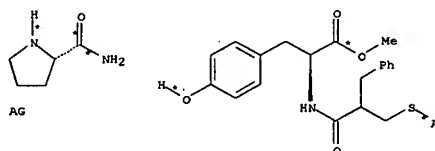
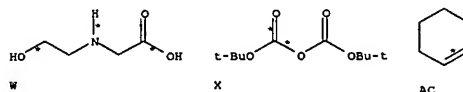
PRO BG 752218-25-0

RX(20) RCT BG 752218-25-0
 RGT F 76-05-1 F3CCO2H
 PRO A 752218-27-2
 SOL 7732-18-5 Water
 CON 3 hours, room temperature

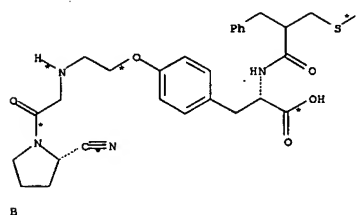
RX(1) RCT A 752218-27-2
 RGT C 1310-65-2 LiOH
 PRO B 752218-29-4
 SOL 109-99-9 THF
 CON 24 hours, room temperature

L12 ANSWER 1 OF 2 CASREACT COPYRIGHT 2008 ACS on STN (Continued)

RX(256) OF 361 COMPOSED OF RX(10), RX(11), RX(12), RX(13), RX(14), RX(19),
 RX(20), RX(1)
 RX(256) W + X + AC + AG + BC ==> B



8
 STEPS



RX(10) RCT W 5835-28-9, X 24424-99-5

STAGE(1)
 RGT Z 1310-73-2 NaOH

L12 ANSWER 1 OF 2 CASREACT COPYRIGHT 2008 ACS on STN (Continued)

SOL 7732-18-5 Water, 123-91-1 Dioxane
 CON 24 hours, room temperature

STAGE(2)
 RGT AA 7647-01-0 HCl
 SOL 7732-18-5 Water

PRO Y 189160-67-6

RX(11) RCT Y 189160-67-6, AC 110-87-2
 RGT AE 9037-24-5 Amberlyst 15
 PRO AD 752218-12-5
 SOL 75-09-2 CH2Cl2
 CON 24 hours, room temperature

RX(12) RCT AD 752218-12-5, AG 7531-52-4
 RGT AI 538-75-0 DCC, AJ 2592-95-2 1-Benzotriazolol, AK 109-02-4
 N-Methylmorpholine
 PRO AH 877373-92-7
 SOL 75-09-2 CH2Cl2
 CON 24 hours, room temperature

RX(13) RCT AH 877373-92-7

STAGE(1)
 RGT AM 288-32-4 1H-Imidazole
 SOL 110-86-1 Pyridine
 CON SUBSTAGE(1) room temperature
 SUBSTAGE(2) room temperature -> -5 deg C

STAGE(2)
 RGT AN 10025-87-3 POC13
 CON SUBSTAGE(1) -5 deg C
 SUBSTAGE(2) -5 deg C -> room temperature

PRO AL 752218-16-9

RX(14) RCT AL 752218-16-9
 RGT AQ 24057-28-1 Pyridinium tosylate
 PRO AP 752218-18-1
 SOL 64-17-5 EtOH
 CON 6 hours, 60 deg C

RX(19) RCT AP 752218-18-1

STAGE(1)
 RGT BH 603-35-0 PPh3, BI 1972-28-7 EtO2CN:NCO2Et
 SOL 109-99-9 THF
 CON 1 hour, room temperature

STAGE(2)
 RCT BC 124735-31-5
 CON 2 days, room temperature

STAGE(3)
 RGT BH 603-35-0 PPh3, BI 1972-28-7 EtO2CN:NCO2Et
 CON 24 hours, room temperature

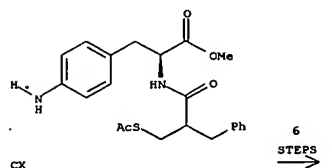
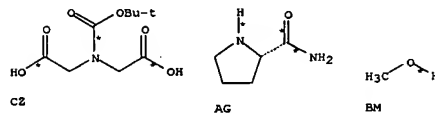
PRO BG 752218-25-0

L12 ANSWER 1 OF 2 CASREACT COPYRIGHT 2008 ACS on STN (Continued)

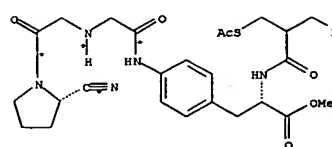
RX(20) RCT BG 752218-25-0
 RGT F 76-05-1 F3CCO2H
 PRO A 752218-27-2
 SOL 7732-18-5 Water
 CON 3 hours, room temperature

RX(1) RCT A 752218-27-2
 RGT C 1310-65-2 LiOH
 PRO B 752218-29-4
 SOL 109-99-9 THF
 CON 24 hours, room temperature

RX(350) OF 361 COMPOSED OF RX(48), RX(49), RX(50), RX(51), RX(52), RX(53)
 RX(350) CZ + AG + BM + CX ==> O



6
 STEPS



L12 ANSWER 1 OF 2 CASREACT COPYRIGHT 2008 ACS on STN (Continued)
RX(48) RCT CZ 56074-20-5

STAGE(1)
RGT AI 538-75-0 DCC
SOL 109-99-9 THF
CON overnight, room temperature

STAGE(2)
RCT AG 7531-52-4
CON 3 hours, room temperature -> 50 deg C

PRO DA 877374-12-4

RX(49) RCT DA 877374-12-4, BM 67-56-1
RGT CO 1122-58-3 4-DMAP, CD 25952-53-8 EDAP
PRO DB 877374-13-5
SOL 75-09-2 CH2Cl2
CON overnight, room temperature

RX(50) RCT DB 877374-13-5

STAGE(1)
SOL 110-86-1 Pyridine
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> -20 deg C

STAGE(2)
RGT AN 10025-87-3 POC13, AM 288-32-4 1H-Imidazole
CON SUBSTAGE(1) -20 deg C
SUBSTAGE(2) -20 deg C -> room temperature

PRO DC 877374-14-6

RX(51) RCT DC 877374-14-6

STAGE(1)
RGT C 1310-65-2 LiOH
SOL 7732-18-5 Water, 109-99-9 THF
CON 4 hours, room temperature

STAGE(2)
RGT BL 7681-38-1 NaHSO4
SOL 7732-18-5 Water

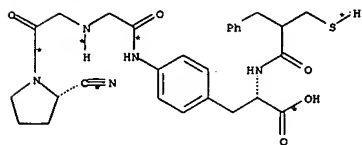
PRO DD 877374-15-7

RX(52) RCT CX 877374-09-9, DD 877374-15-7

STAGE(1)
SOL 110-86-1 Pyridine
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> -20 deg C

STAGE(2)
RGT AN 10025-87-3 POC13

L12 ANSWER 1 OF 2 CASREACT COPYRIGHT 2008 ACS on STN (Continued)



P

RX(48) RCT CZ 56074-20-5

STAGE(1)
RGT AI 538-75-0 DCC
SOL 109-99-9 THF
CON overnight, room temperature

STAGE(2)
RCT AG 7531-52-4
CON 3 hours, room temperature -> 50 deg C

PRO DA 877374-12-4

RX(49) RCT DA 877374-12-4, BM 67-56-1
RGT CO 1122-58-3 4-DMAP, CD 25952-53-8 EDAP
PRO DB 877374-13-5
SOL 75-09-2 CH2Cl2
CON overnight, room temperature

RX(50) RCT DB 877374-13-5

STAGE(1)
SOL 110-86-1 Pyridine
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> -20 deg C

STAGE(2)
RGT AN 10025-87-3 POC13, AM 288-32-4 1H-Imidazole
CON SUBSTAGE(1) -20 deg C
SUBSTAGE(2) -20 deg C -> room temperature

PRO DC 877374-14-6

RX(51) RCT DC 877374-14-6

STAGE(1)
RGT C 1310-65-2 LiOH
SOL 7732-18-5 Water, 109-99-9 THF
CON 4 hours, room temperature

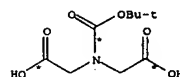
STAGE(2)
RGT BL 7681-38-1 NaHSO4
SOL 7732-18-5 Water

L12 ANSWER 1 OF 2 CASREACT COPYRIGHT 2008 ACS on STN (Continued)
CON SUBSTAGE(1) 1 hour, -20 deg C
SUBSTAGE(2) overnight, -20 deg C -> room temperature

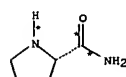
PRO DE 877374-16-8

RX(53) RCT DE 877374-16-8
RGT F 76-05-1 F3CCO2H
PRO O 877374-17-9
SOL 7732-18-5 Water
CON 5 hours, room temperature

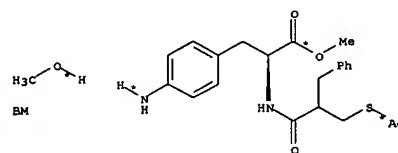
RX(353) OF 361 COMPOSED OF RX(48), RX(49), RX(50), RX(51), RX(52), RX(53),
RX(6)
RX(353) CZ + AG + BM + CX ==> P



CZ



AG



BM

CX

7
STEPS

L12 ANSWER 1 OF 2 CASREACT COPYRIGHT 2008 ACS on STN (Continued)

PRO DD 877374-15-7

RX(52) RCT CX 877374-09-9, DD 877374-15-7

STAGE(1)
SOL 110-86-1 Pyridine
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> -20 deg C

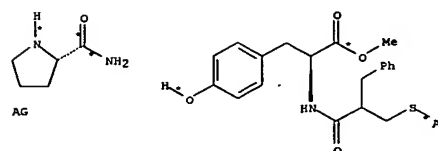
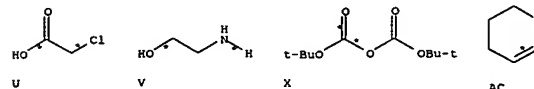
STAGE(2)
RGT AN 10025-87-3 POC13
CON SUBSTAGE(1) 1 hour, -20 deg C
SUBSTAGE(2) overnight, -20 deg C -> room temperature

PRO DE 877374-16-8

RX(53) RCT DE 877374-16-8
RGT F 76-05-1 F3CCO2H
PRO O 877374-17-9
SOL 7732-18-5 Water
CON 5 hours, room temperature

RX(6) RCT O 877374-17-9
RGT C 1310-65-2 LiOH
PRO P 877373-89-2
SOL 7732-18-5 Water, 109-99-9 THF
CON 4 hours, room temperature

RX(358) OF 361 COMPOSED OF RX(9), RX(10), RX(11), RX(12), RX(13), RX(14),
RX(19), RX(20), RX(1)
RX(358) U + V + X + AC + AG + BC ==> B

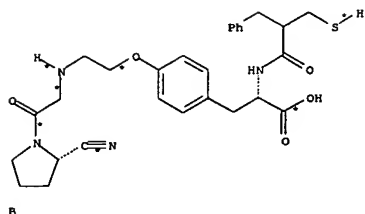


AG

BC

9
STEPS

L12 ANSWER 1 OF 2 CASREACT COPYRIGHT 2008 ACS on STN (Continued)



RX(9) RCT U 79-11-8, V 141-43-5
PRO W 5835-28-9
SOL 7732-18-5 Water
CON 24 hours, room temperature

RX(10) RCT W 5835-28-9, X 24424-99-5

STAGE(1)
RGT Z 1310-73-2 NaOH
SOL 7732-18-5 Water, 123-91-1 Dioxane
CON 24 hours, room temperature

STAGE(2)
RGT AA 7647-01-0 HCl
SOL 7732-18-5 Water

PRO Y 189160-67-6

RX(11) RCT Y 189160-67-6, AC 110-87-2
RGT AE 9037-24-5 Amberlyst 15
PRO AD 752218-12-5
SOL 75-09-2 CH2Cl2
CON 24 hours, room temperature

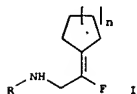
RX(12) RCT AD 752218-12-5, AG 7531-52-4
RGT AI 538-75-0 DCC, AJ 2592-95-2 1-Benzotriazolol, AK 109-02-4
N-Methylmorpholine
PRO AH 877373-92-7
SOL 75-09-2 CH2Cl2
CON 24 hours, room temperature

RX(13) RCT AH 877373-92-7

STAGE(1)

L12 ANSWER 2 OF 2 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 142:218971 CASREACT
TITLE: Fluoro-Olefins as Peptidomimetic Inhibitors of Dipeptidyl Peptidases
AUTHOR(S): Van der Veken, Pieter; Senten, Kristel; Kertesz, Istvan; De Meester, Ingrid; Lambert, Anne-Marie;
Maes, Marie-Berthe; Scharpe, Simon; Haemers, Achiel; Augustyns, Koen
CORPORATE SOURCE: Departments of Medicinal Chemistry and Medical Biochemistry, University of Antwerp, Antwerp, Belgium
SOURCE: Journal of Medicinal Chemistry (2005), 48(6), 1768-1780
CODEN: JMCNAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB The feasibility of the fluoro-olefin function as a peptidomimetic group in inhibitors for dipeptidyl peptidase IV and II (DPP IV and DPP II) is investigated by evaluation of N-substituted Gly-V[CF(C)]pyrrolidines, Gly-V[CF(C)]piperidines (i.e., I and II with R = cyclohexyl, PhCH2, 4-benzyl-4-piperidyl, etc.) and Gly-V[CF(C)](2-cyano)pyrrolidines. Of this later class, the (Z)- and (E)-fluoro-olefin analogs were prepared and chemical stability in comparison with the parent amide was checked. Most of these compds. exhibited a strong binding preference toward DPP II with IC50 values in the low micromolar range, while only low DPP IV inhibitory potential is seen.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS
FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

RX(79) OF 237 AN + DI + EG ==> EH

L12 ANSWER 1 OF 2 CASREACT COPYRIGHT 2008 ACS on STN (Continued)

RGT AM 288-32-4 1H-Imidazole
SOL 110-86-1 Pyridine
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) room temperature -> -5 deg C

STAGE(2)
RGT AN 10025-87-3 POC13
CON SUBSTAGE(1) -5 deg C
SUBSTAGE(2) -5 deg C -> room temperature

FRO AL 752218-16-9

RX(14) RCT AL 752218-16-9
RGT AQ 24057-28-1 Pyridinium tosylate
FRO AF 752218-18-1
SOL 64-17-5 EtOH
CON 6 hours, 60 deg C

RX(19) RCT AP 752218-18-1

STAGE(1)
RGT BH 603-35-0 PPh3, BI 1972-28-7 EtO2CN:NCO2Et
SOL 109-99-9 THF
CON 1 hour, room temperature

STAGE(2)
RGT BC 124735-31-5
CON 2 days, room temperature

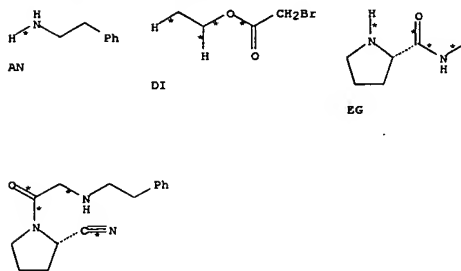
STAGE(3)
RGT BH 603-35-0 PPh3, BI 1972-28-7 EtO2CN:NCO2Et
CON 24 hours, room temperature

PRO BG 752218-25-0

RX(20) RCT BG 752218-25-0
RGT F 76-05-1 F3CCO2H
FRO A 752218-27-2
SOL 7732-18-5 Water
CON 3 hours, room temperature

RX(1) RCT A 752218-27-2
RGT C 1310-65-2 LiOH
PRO B 752218-29-4
SOL 109-99-9 THF
CON 24 hours, room temperature

L12 ANSWER 2 OF 2 CASREACT COPYRIGHT 2008 ACS on STN (Continued)



EH
YIELD 42%

RX(79) RCT AN 64-04-0

STAGE(1)
RGT BW 24424-99-5 (Boc)2O
SOL 75-09-2 CH2Cl2

STAGE(2)
RGT DI 105-36-2
SOL 60-29-7 Et2O

STAGE(3)
RGT EG 7531-52-4
SOL 60-29-7 Et2O
CON SUBSTAGE(1) -5 deg C
SUBSTAGE(2) 4 hours, room temperature

STAGE(4)
RGT AB 7631-86-9 SiO2
CON room temperature

STAGE(5)
RGT BY 288-32-4 1H-Imidazole
SOL 110-86-1 Pyridine
CON room temperature -> -10 deg C

STAGE(6)
RGT AC 10025-87-3 POC13
SOL 75-09-2 CH2Cl2
CON 15 minutes, -10 deg C

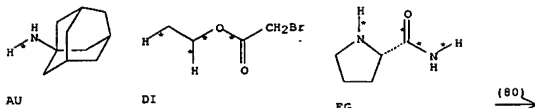
STAGE(7)
RGT AB 7631-86-9 SiO2
CON room temperature

L12 ANSWER 2 OF 2 CASREACT COPYRIGHT 2008 ACS on STN (Continued)

STAGE(8)
 RGT CU 76-05-1 F3CCO2H
 SOL 75-09-2 CH2Cl2
 CON 15 minutes, room temperature

PRO EH 437702-73-3

RX(80) OF 237 AU + DI + EG ==> EI



EI
 YIELD 38%

RX(80) RCT AU 768-94-5

STAGE(1)
 RGT BW 24424-99-5 (Boc)2O
 SOL 75-09-2 CH2Cl2

STAGE(2)
 RGT DI 105-36-2
 SOL 60-29-7 Et2O

STAGE(3)
 RGT EG 7531-52-4
 SOL 60-29-7 Et2O
 CON SUBSTAGE(1) -5 deg C
 SUBSTAGE(2) 4 hours, room temperature

STAGE(4)
 RGT AB 7631-86-9 SiO2
 CON room temperature

L12 ANSWER 2 OF 2 CASREACT COPYRIGHT 2008 ACS on STN (Continued)

RCT DI 105-36-2
 SOL 60-29-7 Et2O

STAGE(3)
 RGT EG 7531-52-4
 SOL 60-29-7 Et2O
 CON SUBSTAGE(1) -5 deg C
 SUBSTAGE(2) 4 hours, room temperature

STAGE(4)
 RGT AB 7631-86-9 SiO2
 CON room temperature

STAGE(5)
 RGT BY 288-32-4 1H-Imidazole
 SOL 110-86-1 Pyridine
 CON room temperature -> -10 deg C

STAGE(6)
 RGT AC 10025-87-3 POCl3
 SOL 75-09-2 CH2Cl2
 CON 15 minutes, -10 deg C

STAGE(7)
 RGT AB 7631-86-9 SiO2
 CON room temperature

STAGE(8)
 RGT CU 76-05-1 F3CCO2H
 SOL 75-09-2 CH2Cl2
 CON 15 minutes, room temperature

PRO EJ 777946-69-7

L12 ANSWER 2 OF 2 CASREACT COPYRIGHT 2008 ACS on STN (Continued)

STAGE(5)
 RGT BY 288-32-4 1H-Imidazole
 SOL 110-86-1 Pyridine
 CON room temperature -> -10 deg C

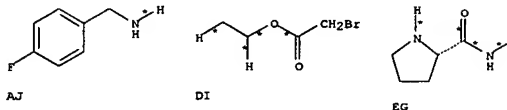
STAGE(6)
 RGT AC 10025-87-3 POCl3
 SOL 75-09-2 CH2Cl2
 CON 15 minutes, -10 deg C

STAGE(7)
 RGT AB 7631-86-9 SiO2
 CON room temperature

STAGE(8)
 RGT CU 76-05-1 F3CCO2H
 SOL 75-09-2 CH2Cl2
 CON 15 minutes, room temperature

PRO EI 741657-02-3

RX(81) OF 237 AJ + DI + EG ==> EJ



EJ
 YIELD 48%

RX(81) RCT AJ 140-75-0

STAGE(1)
 RGT BW 24424-99-5 (Boc)2O
 SOL 75-09-2 CH2Cl2

STAGE(2)